Genetic Tagging During Human Mesoderm Differentiation Reveals Tripotent Lateral Plate Mesodermal Progenitors.

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Public Summary:

Although clonal studies of lineage potential have been extensively applied to organ specific stem and progenitor cells, much less is known about the clonal origins of lineages formed from the germ layers in early embryogenesis. We applied lentiviral tagging followed by vector integration site analysis (VISA) with high-throughput sequencing to investigate the ontogeny of the hematopoietic, endothelial and mesenchymal lineages as they emerge from human embryonic mesoderm. In contrast to studies that have used VISA to track differentiation of self-renewing stem cell clones that amplify significantly over time, we focused on a population of progenitor clones with limited self-renewal capability. Our analyses uncovered the critical influence of sampling on the interpretation of lentiviral tag sharing, particularly among complex populations with minimal clonal duplication. By applying a quantitative framework to estimate the degree of undersampling we revealed the existence of tripotent mesodermal progenitors derived from pluripotent stem cells, and the subsequent bifurcation of their differentiation into bipotent endothelial/hematopoietic or endothelial/mesenchymal progenitors.

Scientific Abstract:

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